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Short Note

Diagnosis and Management of Goiter in an Atlantic Walrus (*Odobenus rosmarus rosmarus*)

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A 15-y-old aquarium-housed female Atlantic walrus (*Odobenus rosmarus rosmarus*) presented with a non-painful cervical mass that had enlarged over a few months (Figure 1). The walrus was fed daily with a diet composed on average of 8 kg mackerel (*Scomber* sp.), 6 kg herring (*Clupea* sp.), 2 kg capelin (*Mallotus villosus*), 2 kg squid (*Illex illecebrosus*), 0.8 kg shrimp (*Pandalus borealis*), 0.8 kg krill, 0.3 kg mussels (*Mytilus edulis*), and a vitamin supplement (8 tablets per day, Opti-Marine; Animal Necessity, Key Largo, FL, USA). The walrus was housed with two adult Pacific walruses (*Odobenus rosmarus divergens*) in artificial saltwater with a salinity of 27 g/L, reconstituted with sodium bicarbonate salt (Hi Grade granulated salt; Windsor, Pointe-Claire, QC, Canada), and a mix of sodium bicarbonate and potassium chloride (Kali Sel; K+S, Chicago, IL, USA). The potassium concentration ranged from 130 to 412 mg/L in the main pool. The life support system included a sand filter, chlorine disinfection, and an ozone tower. Previous medical history included a gestation 2 y prior and a mild chronic unilateral lameness of the right pelvic limb, with no associated skeletal lesion on historical radiographs. During gestation and lactation, the walrus was supplemented with iodine at 850 µg/d (1,000 mg Varech containing 850 µg of iodine, Swiss Natural; Valeant Pharmaceuticals International, Inc., Laval, QC, Canada), calcium at 2.8 mg/kg/d, and vitamin D3 at 4 UI/kg/d (650 mg calcium, D3 400 UI, and D3 1,000 UI; Jamiesson, Windsor, ON, Canada) for approximately 1.5 y.

On physical examination, the walrus weighed 650 kg and had an adequate body condition score. The cervical mass was ventral, non-fluctuating, soft on palpation, and did not appear painful as the walrus was able to lie in ventral recumbency with her head on the ground. Differential diagnoses for the cervical mass included laryngeal pouch abscess; thyroid hyperplasia or neoplasia; subcutaneous abscess; lipoma or other soft tissue neoplasm; and salivary gland abscess, neoplasm, or hyperplasia.

Cervical ultrasound (2-5 MHz C60x transducer, Edge Ultrasound System; SonoSite Inc., Bothell, WA, USA) was conducted voluntarily with biomedical training. Bilateral masses were located 2.5 to 5 cm from the skin surface and were non-adherent to deep tissue planes. These masses were hypoechoic compared to surrounding adipose tissues, contained a moderate vascular component on color doppler examination with multiple cystic foci, and were delineated by a well-demarcated capsule. The echogenicity and architectural characteristics of these masses and localization in relation to the carotid artery were consistent with thyroid tissue (Taeymans et al., 2007). On the left side, a vessel caudal to the mass, with a blood flow compatible with a branch of the carotid artery, was oriented perpendicularly to the vertebral column. This orientation is unusual for a branch of the carotid artery; thus, a mass effect was suspected. Within 10 mo, the mass increased from 10 to greater than 25 cm in diameter (Figure 2). The cranio-caudal

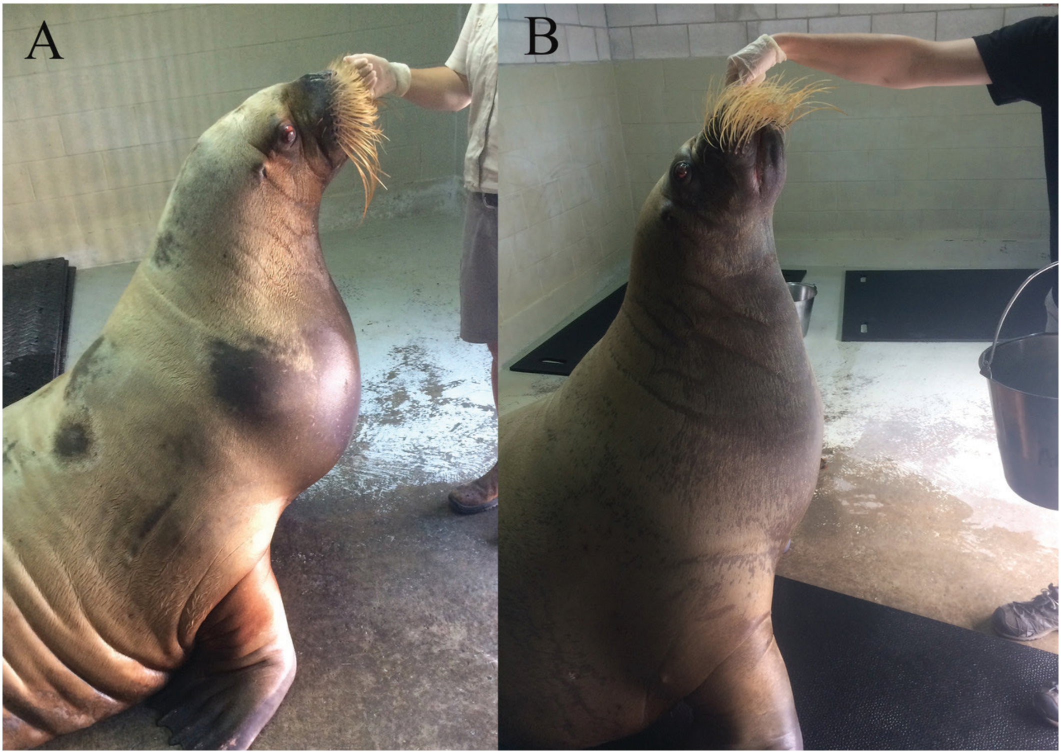

Figure 1. (A) Cervical enlargement in a female Atlantic walrus (*Odobenus rosmarus rosmarus*) on presentation and (B) 8 mo later while treated with levothyroxine. While goiter was bilateral, the right side of the patient is shown.

length of the mass was greater than 20 cm and too large to be measured by ultrasound. In comparison, thyroid diameter measured by cervical ultrasound in a 1,000-kg male conspecific was 6.9 cm in depth by 9.34 cm in length. Three fine needle aspirations were performed over a 1-mo period under operant conditioning using a 22-gauge, 2.5" spinal needle. Staining was performed with Diff Quick (Jorvet; Jorgensen Labs, Loveland, CO, USA). Cytologic examination was inconclusive; only adipose tissue was visualized.

Blood samples were obtained from the caudal gluteal vein and from interdigital veins of the left pelvic limb under operant conditioning using a 25-gauge needle mounted on a 1- to 3-mL syringe. Hematology and plasma biochemistry were unremarkable compared to the published references range for walruses (Gulland et al., 2018). Total thyroxine (T4) concentrations (9.2 and 9.6 nmol/L) measured by a chemiluminescent competitive immunoassay (Canine total T4, IMMULITE®; Diagnostic Products Corporation, Los Angeles, CA, USA) were markedly lower than values obtained in free-ranging walruses (mean ± standard deviation [SD]: 76 ± 24 nmol/L; n = 38; Routti et al., 2019). Serum thyroid-stimulating hormone (TSH) concentrations were measured with a commercially available test (IMMULITE®, Diagnostic Products Corporation). A value of 7.51 ng/mL was obtained, which was interpreted as markedly increased compared to values obtained with the same assay in three other aquarium-housed walruses (range: 0.06 to 1.01 ng/ml; n = 7 samples, including conspecifics in the same enclosure). Based on these observations, hypothyroidism associated with hyperplastic thyroid glands or thyroiditis was suspected.

Total dietary iodine and selenium intake from the diet was estimated by analyzing food items by a commercial laboratory (Shur Gain, St. Hyacinthe, QC, Canada). This estimate was compared to those expected in free-ranging walruses feeding mostly on bivalves (Table 1). This comparison showed that the estimated daily iodine intake was lower in this walrus under human care. Thus, iodine deficiency was suspected. Conversely, selenium intake was higher in the present case than the theoretical intake in walruses that would feed exclusively on clams. Indeed, mackerel, the main item of the diet, had a selenium content of 0.89 mg/kg as sampled, while clams had a selenium content of 0.41 mg/kg as sampled. Iodine supplementation was implemented at a dose of 0.6 µg/kg/d for a week (0.5

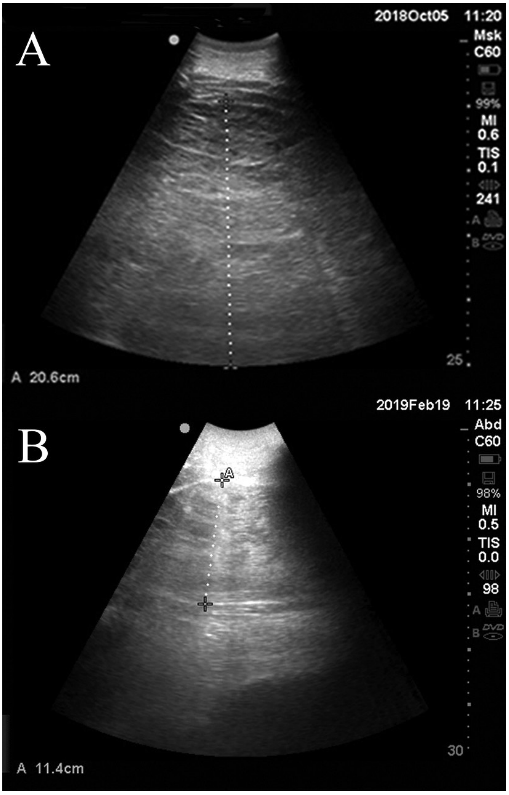

Figure 2. Ultrasonographic images of a glandular encapsulated organ in the left cervical area of an Atlantic walrus: Figure 2A was obtained just prior to initiation of levothyroxine treatment while the mass measured more than 20.6 cm in diameter (delineated by the cross markers); and Figure 2B was obtained at the same level after 4 mo of treatment with levothyroxine. At this point, tissue was less cystic, and the mass was 11.4 cm in diameter (delineated by the cross markers). Note that the scale of each ultrasound is different.

tablet of 1,000 mg Varech containing 850 µg of iodine, Swiss Natural, Valeant Pharmaceuticals International, Inc.), and then 1.2 µg/kg/d for 5 mo. Urinary iodine concentration measured on a urinary sample obtained prior to iodine supplementation at the Centre de Toxicologie du Québec of the Institut National de Santé Publique du Québec was 2.9 µmol/L (358 µg/L). While no reference value for urinary iodine is available for walruses, urinary iodine of the clinically healthy conspecific was 1.5 µmol/L (241 µg/L). In humans, urinary values above 2.37 µmol/L (300 µg/L) are considered indicative of excessive iodine intake (Leung & Braverman, 2014). While these results were more consistent with an excess of dietary iodine, the main clinical suspicion remained iodine deficiency due to the lack of reference values in walruses. The cervical mass diameter monitored on ultrasound continued to increase in volume despite iodine supplementation (Figure 3), and medical management was revised.

At this time, pregnancy was suspected in this walrus based on hormonal test results. Therefore, it was decided to initiate treatment with levothyroxine in an attempt to quickly resolve hypothyroidism, which can affect neurological development in the fetus. Levothyroxine (12 mg Thyro-L per teaspoon; Loyd Inc., Shenandoah, IA, USA) was prescribed at 0.01 mg/kg orally once a day. The levothyroxine dose was gradually increased with follow-up TSH-level measurements every 3 wks after dose adjustment. A maintenance dose of 0.02 mg/kg orally twice daily produced a reduction of TSH concentration to 0.11 ng/mL. Concomitantly, due to the suspicion of iodine excess based on urinary iodine concentration, nutritional modifications were implemented to decrease dietary iodine concentration, including a switch to a mineral supplement without iodine (Mazuri marine mammal with lutein; Mazuri, St. Louis, MO, USA) and a decrease of proportions of mackerel and mussels in the diet. Figure 4 illustrates the evolution of the levothyroxine dose, TSH concentration, and mass diameter measured on ultrasound. The diameter of the thyroidal mass decreased to 10 cm in diameter within 4 mo of treatment with levothyroxine (Figure 3). Improvement of the right pelvic limb lameness was also noted.

The walrus has received levothyroxine for the past 10 mo and is clinically stable. Biochemistry and hematology parameters remain within normal limits (Gulland et al., 2018). In one instance, the levothyroxine dose was decreased by half (to 0.02 mg/kg/d) because TSH was decreased to 0.27 ng/mL, and weight gain was considered suboptimal for the time of year. The walrus developed constipation and dysorexia within 10 d, which resolved after re-increasing the levothyroxine dose to 0.03 mg/kg/d after 3 wks of persistent constipation despite oral mineral oil (Rougier Pharma, Mirabel, QC, Canada) administration.

In contrast to the diet of aquarium-housed walruses, most free-ranging walruses are reported to eat mostly bivalves with occasional fish (Sheffield & Grebmeier, 2009). In addition, some walruses may rarely eat smaller pinnipeds, cetaceans, and seabirds (Scotter et al., 2019). In an attempt to decrease the cholesterol content of the diet and to transition the animals to a feeding regime closer to the one of free-ranging walruses, clams were introduced into the daily diet of these walruses, while the proportion of high-iodine fish was decreased. Clams were also analyzed for

Table 1. Estimated total dietary iodine daily intake based on concentration as sampled; measured by Shur Gain, a commercial laboratory; and calculated in function of daily intake

	Concentration of iodine (measured in mg as sampled)	Iodine dose ingested daily in mg/kg body weight (estimated)
Captive daily diet		
Mackerel (/kg product)	0.8	7.0
Herring (/kg product)	0.07	0.5
Mussel (/kg product)	1.8	1.0
Opti-Marine (/tablet)	0.15	1.2
Varech (/tablet)	0.85	1.2
Captive diet total		10.9
Theoretical daily diet of free-ranging walruses eating 100% clams		
Clams	2.04	28.0

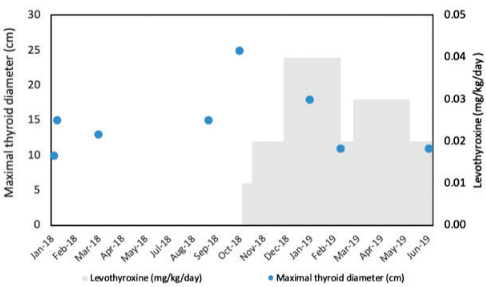

Figure 3. Progression of left-sided mass diameter measured by ultrasonography and levothyroxine dose administered concomitantly in a female Atlantic walrus

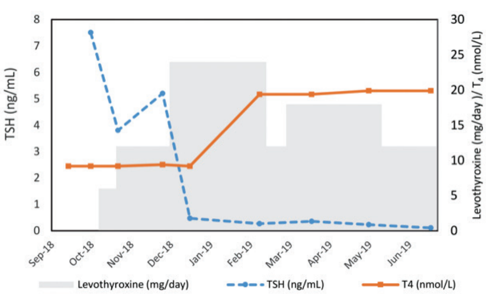

Figure 4. Evolution of thyroid stimulating hormone (TSH) and thyroxine (T4) serum concentrations in relation to daily levothyroxine supplementation in a female Atlantic walrus

comparison to the previously offered diet. In this case, it was not possible to clearly identify a nutritional factor causing the thyroid goiter. Other walruses of this group received a similar fish-based diet, although individual preferences were noted for mackerel or herring. Thus, a generic approach of supplementation with levothyroxine was undertaken as previously reported in human medicine (Wilders-Truschnig et al., 1993). In hypothyroid humans with iodine deficiency, supplementation with levothyroxine has been shown to be safe and to reduce thyroid size (Wilders-Truschnig et al., 1993). In the same study, TSH concentration was not statistically correlated with thyroid size but was reduced by levothyroxine administration, similar to what was observed in this walrus.

Various nutritional factors have been associated with hypothyroidism, including iodine, zinc, iron deficiency or excess, selenium, and calcium (Köhrle, 2015). Zinc and iron deficiency were considered unlikely since hematocrit was within the reference range reported for Pacific walruses (Gulland et al., 2018). Calcium deficiency was also considered unlikely given that the whole-prey diet provided high calcium concentration, and the female had received vitamin D and calcium during gestation and lactation. Selenium deficiency was considered unlikely as the estimated selenium concentration of the diet of this animal was higher than the theoretical concentration in free-ranging walruses feeding mainly on bivalves. The therapeutic trial performed with iodine in this case was unsuccessful, which could be because excessive iodine was actually the cause of the observed goiter. Alternatively, it is possible that iodine dose or supplementation duration of 3 mo was insufficient to observe a reduction of the thyroid volume. Iodine deficiency is a commonly reported cause of hypothyroidism. However, iodine excess can also be a predisposing factor for autoimmune thyroid disorders (Luo et al., 2014) and thyroid tumors in humans (Lee et al., 2017). Hence, it was not possible to definitively rule out iodine deficiency or iodine excess in the case presented herein. No attempt was made to measure anti-thyroglobulin antibodies in this case as this is a species-specific test, which is not available in walruses. It should also be noted that free-ranging walruses live in seawater containing iodine, which was not the case in this aquarium. The impact of housing walruses in artificial saltwater devoid of iodine has not been studied at this point.

Thyroid hormones play a critical role in the metabolism, homeostasis, neurodevelopment, and protein synthesis in mammals (Kunisue et al., 2011). Hypothyroidism may be associated with lethargy, dermatologic lesions such as alopecia, weight gain, peripheral neuropathy, and constipation (Budsberg & Moore, 1993; Scott-Moncrieff, 2010). Possible clinical signs compatible with hypothyroidism in this walrus included cervical mass, intermittent constipation noted when levothyroxine dose was decreased, and pelvic lameness of unknown origin which improved with levothyroxine treatment. No dermatological signs were observed except occasional self-resolving localized cutaneous furonculosis. Of note, hypothyroid dogs are predisposed to recurring infection of the skin (Scott-Moncrieff, 2010). Body weight was challenging to interpret in this walrus as a pregnancy was suspected based on abdominal ultrasound at the time of treatment. Indeed, this suspicion prompted the initiation of treatment with levothyroxine as maternal hypothyroidism can impact fetal development (Liu et al., 2018) and is associated with dystocia (Hernandez et al., 2018), uterine inertia, and spontaneous abortion (Scott-Moncrieff, 2010).

Thyroxine concentrations were challenging to interpret in this case. Indeed, reference intervals for thyroxine and TSH have not been published in walruses. Values obtained from free-ranging walruses were measured with a different assay (EIAgen enzyme-linked immunosorbent assays; Diagnostics Biochem Canada Inc., London, ON, Canada) and were not directly comparable with values obtained with our assay. Total thyroxine values were at the lower end of the T4 range obtained with the same assay in three other aquarium-housed walruses. Reference intervals for T4 established in elephant seals (*Mirounga angustirostris*; mean ± SD: 54 ± 2.3 nmol/L; n = 144; Jelincic et al., 2017) and Steller sea lions (*Eumetopias jubatus*; mean ± SD: 18.53 ± 0.7 nmol/L; n = 160; Myers et al., 2006) were markedly higher than those reported in this case, but this could be due to the use of different assays or to interspecific variabilities. However, a low correlation has been noted between T4 measurements with an electrochemilumiscent immunoassay and liquid chromatography tandem mass spectrometry in Baikal seals (*Pusa siberica*; Kunisue et al., 2011). Regardless, the progression of thyroxine concentration made clinical sense as total thyroxine increased while TSH decreased during levothyroxine administration. Measurement of free thyroxine concentration was attempted in this case but was complicated by border regulations. Therefore, it was elected to monitor TSH and mass diameter in this case rather than total T4 concentration. The observed decrease of TSH during levothyroxine treatment suggests at least partial cross-reactivity between canine and walrus TSH. Arterial blood pressure could not be measured in this case; therefore, repeat biochemistry panels were performed to monitor renal function as kidneys could be affected by hypertension in the case of levothyroxine overdose (Mariani & Berns, 2012).

Thyroid lesions have been reported anecdotally in walruses housed in zoological institutions, including a hyperplastic thyroid in association with atherosclerotic lesions of thyroid vessels in another female walrus in the same institution. A limitation of this case is that histology of the lesion could not be obtained, which may have allowed better characterization of the lesion. However, the present case suggests that thyroid hyperplastic lesions should be considered in the presence of cervical enlargement in this species.

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